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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/711,476 | 11/13/2000 | C. Thomas Caskey | 2875.1001-007 | 8353 |

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| EXAMINER | |
|---|---|
| FREDMAN, JEFFREY NORMAN | |
| ART UNIT | PAPER NUMBER |
| 1637 | |

DATE MAILED: 06/17/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/711,476 | CASKEY ET AL. | |
| | Examiner | Art Unit | |
| | Jeffrey Fredman | 1637 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *12 May 2004* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *42 and 54-65* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *42* is/are allowed.

6)☒ Claim(s) *54-64* is/are rejected.

7)☒ Claim(s) *65* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *attached* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

## DETAILED ACTION

### *Continued Examination Under 37 CFR 1.114*

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on May 12, 2004 has been entered.

### *Claim Rejections - 35 USC § 102*

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

3. Claims 54-63 are rejected under 35 U.S.C. 102(b) and (e) as being anticipated by Soderlund (U.S. Patent 6,013,431) and Soderlund (WO 91/13075).

For ease of reference, the U.S. patent will be referred to for the rejection, but the Soderlund WO is identical in disclosure. This new rejection was necessitated by Applicant's amendment.

Soderlund teaches a method of analyzing a polynucleotide of interest for the presence or absence of an altered region (see abstract and preamble of claim 1, column 18) comprising the steps of:

a) annealing a single sample of the polynucleotide of interest to a plurality of primers (see column 9, lines 14-32, where a single sample is split into two tubes and annealed to two different primers (two being a plurality)), wherein the primers comprise an array of consecutive single stranded oligonucleotides having known sequences (see figure 3, primer 1 and primer 2) wherein each primer differs from the previous primer in the array by one base at the 3' end (see figure 3, primer 1 and primer 2) and wherein the primers are capable of hybridizing successively along the polynucleotide of interest, generating a plurality of annealed primers (see figure 3)

b) subjecting the primer complexes to a single base extension reaction using a polymerase to extend the annealed primers by the addition of a terminating nucleotide, generating a plurality of extended primers (see figure 3, where the terminator is ddY1, for example as well as column 8, lines 31-39 and columns 9-11),

c) observing the identity of each terminating nucleotide that has been added to each extended primer, thereby determining the identity of at least one nucleotide position of a polynucleotide of interest and thereby analyzing the polynucleotide of interest for the presence or absence of an altered region (see figure 3 and example 1, columns 9-11).

With regard to claim 55, Soderlund teaches the use of a polymerase and nucleotides corresponding to the four different bases (see column 8, lines 52-58).

With regard to claims 56-58, Soderlund teaches the use of multiple differentially labeled nucleotides (see column 8, lines 58-60 and column 19, claim 17).

Also, with regard to claim 58, Soderlund teaches the use of fluorescent labels (see column 18, claim 8).

With regard to claim 59, Soderlund teaches analyzing either the coding or complementary non coding strands of a polynucleotide of interest (see abstract).

With regard to claim 60, Soderulund teaches the use of ddNTPs (see column 18, claim 6).

With regard to claims 61 and 62, Soderlund teaches primers between 14 and 40 bases (see column 6, lines 42-45) and exemplifies 20 mers (see column 9, line 66, primer D1, which is 20 nucleotides in length).

With regard to claim 63, Soderlund teaches primers of different lengths (see figure 3, primer 1 and primers 2 and 3 are of different lengths).

***Claim Rejections - 35 USC § 103***

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein

were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

6. Claims 54-64 are rejected under 35 U.S.C. 103(a) as being unpatentable over either Soderlund (U.S. Patent 6,013,431) or Soderlund (WO 91/13075), either in view of Mackay (U.S. Patent 4,874,492).

Soderlund teaches a method of analyzing a polynucleotide of interest for the presence or absence of an altered region (see abstract and preamble of claim 1, column 18) comprising the steps of:

a) annealing a single sample of the polynucleotide of interest to a plurality of primers (see column 9, lines 14-32, where a single sample is split into two tubes and annealed to two different primers (two being a plurality)), wherein the primers comprise an array of consecutive single stranded oligonucleotides having known sequences (see figure 3, primer 1 and primer 2) wherein each primer differs from the previous primer in the array by one base at the 3' end (see figure 3, primer 1 and primer 2) and wherein the primers are capable of hybridizing successively along the polynucleotide of interest, generating a plurality of annealed primers (see figure 3)

b) subjecting the primer complexes to a single base extension reaction using a polymerase to extend the annealed primers by the addition of a terminating nucleotide,

generating a plurality of extended primers (see figure 3, where the terminator is ddY1, for example as well as column 8, lines 31-39 and columns 9-11),

c) observing the identity of each terminating nucleotide that has been added to each extended primer, thereby determining the identity of at least one nucleotide position of a polynucleotide of interest and thereby analyzing the polynucleotide of interest for the presence or absence of an altered region (see figure 3 and example 1, columns 9-11).

With regard to claim 55, Soderlund teaches the use of a polymerase and nucleotides corresponding to the four different bases (see column 8, lines 52-58).

With regard to claims 56-58, Soderlund teaches the use of multiple differentially labeled nucleotides (see column 8, lines 58-60 and column 19, claim 17).

Also, with regard to claim 58, Soderlund teaches the use of fluorescent labels (see column 18, claim 8).

With regard to claim 59, Soderlund teaches analyzing either the coding or complementary non coding strands of a polynucleotide of interest (see abstract).

With regard to claim 60, Soderulund teaches the use of ddNTPs (see column 18, claim 6).

With regard to claims 61 and 62, Soderlund teaches primers between 14 and 40 bases (see column 6, lines 42-45) and exemplifies 20 mers (see column 9, line 66, primer D1, which is 20 nucleotides in length).

With regard to claim 63, Soderlund teaches primers of different lengths (see figure 3, primer 1 and primers 2 and 3 are of different lengths).

Soderlund does not teach the use of a CCD device or of a photomultiplier for fluorescent detection.

Mackay teaches detection of nucleic acids with a CCD device (see abstract and columns 1 and 2)..

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to utilize the fluorescent detection method of Goelet in the method of Soderlund since Soderlund expressly teaches the use of fluorescent labels and Goelet teaches that such labels can be detected using CCD devices or photomultiplier tubes, stating "The invention enables analysis of the results of electrophoresis to be speeded up significantly as compared with autoradiography techniques, as well as increasing the accuracy obtainable and permitting use of smaller sample volumes than has been possible hitherto. The invention also greatly increases the range of integrated spot or band intensities contained within one array that can be handled, and alows much more accurate quantitation of the amount of say[sic] protein or DNA in each separated spot or band. (see column 4, lines 7-16)." So an ordinary practitioner would have been motivated to detect the fluorescent labels of Soderlund with the well known CCD device in order to improve accuracy, improve the range of intensities that can be detected and increase the speed while decreasing the amount of expensive reagents which are necessary.

***Allowable Subject Matter***

7. The following is a statement of reasons for the indication of allowable subject matter: Amended claim 42 is free of the prior art. The claim is drawn to an embodiment

in which the oligonucleotide array is regenerated by digestion of the newly added nucleotide after completion of the assay. The cited prior art of Soderlund, Goulet, Rust, or Cantor in the IDS, do not teach regeneration of the array by cleavage mechanisms.

8. Claim 65 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims. There is no teaching in Soderlund to use dinucleotides, nor in any of the other cited prior art. Soderlund uses two nucleotides sequentially as in figure 3, but never a single dinucleotide molecule for termination.

### *Response to Arguments*

9. Applicant's arguments filed May 12, 2004 have been fully considered but they are not persuasive.

Applicant argues that Soderlund divides the sample in two, while the claim is drawn to a "single sample". Soderlund also begins with a single sample. The claim is of the open, comprising format and permits additional steps such as separation of the sample into two parts. With regard to the argument that Soderlund does not teach two oligos that differ by one position at the 3' end, Applicant is referred to figure 3 of Soderlund, where such a scenario is expressly disclosed.

The remaining arguments are drawn to rejections that are now withdrawn.

### *Conclusion*

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey Fredman whose telephone number is (571)272-0742. The examiner can normally be reached on 6:30-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571)272-0782. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Jeffrey Fredman
Primary Examiner
Art Unit 1637

6/15/04